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(54) Polymer surfaces for blood-contacting surfaces of a biomedical device and methods for forming

(57) A polymer mixture having a  $\gamma_c$  between 10 and 35 dyne/cm is formed from at least 95 volume % of a base polymer and not greater than 5 volume % of a polymer additive including at least first and second different homopolymer chains in graft or block copolymer form. The first chains are characterized by a low critical surface tension but with a tendency to exude while the second ones lower this tendency. This polymer mixture is formed into the exposed blood-contacting surface of a biochemical device. A preferred additive is a block copolymer of (a) polydialkylsiloxanes and (b) a polyurethane.

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# SPECIFICATION

## Biomedical device with blood-compatible surface

5 One widely accepted hypothesis regarding blood compatibility is that it is maximized within a narrow range of surface free energies which give rise to favourable interactions with plasma proteins. A common measurement of surface free energies is by Zisman's critical surface tension ( $\gamma_c$ ). The optimum value has been found empirically to lie within the range of a  $\gamma_c$  equal to about 20 to 30 dyne/cm., see, e.g., R.A. Baeir, Ann. N.Y. Acad. Sci. 17, 283 (1977).

10 Common polymers (e.g. polyurethane) which provide the desired physical properties for the blood contact surfaces of biomedical devices often do not fall within this range of critical surface tensions.

Polysiloxanes are known to have a particularly low critical surface tension value and have been suggested for incorporation into polyurethanes to improve the surface characteristics of such materials. However, polysiloxane by itself is known to have a tendency to exude from the polyurethane base polymer as illustrated in Reischl et al., U.S. Patent 3,243,475.

Polysiloxane-polyurethane block copolymers have been suggested for use to modify the surface characteristics of blood contact surfaces of devices of biomedical devices as illustrated in Nyilas U.S. Patent 3,562,352. The technique disclosed for such use includes fabricating the entire blood contact devices from such block copolymers or coating such devices with the copolymers. The block copolymers themselves have poor structural characteristics due to a high proportion of polysiloxane. On the other hand, the coated materials are particularly expensive to form as they are not processable by thermoplastic methods such as injection molding and extrusion. The manufacture of tubing, catheters and other blood-contacting disposable devices from such materials is particularly expensive due to the necessity of employing solution fabrication techniques.

Certain experimental work has been published relating to the blending of block copolymers of polydimethylsiloxane with homopolymers of higher critical surface tensions. These materials are known to produce films with high siloxane surface concentrations. See, for example, D.G. Legrand and R.L. Gaines, Jr., Polym Prepr. 11, 442 (1970); D.W. Dwight et al., Polym. Prepr. 20, (1), 702 (1979); and J.J. O'Malley, Polym Prepr. 18 (1977). However, all of these references describe the polymer blends in terms of scientific experiments without suggestion that the material would have any advantage for use in any biomedical application.

In a first aspect the present invention provides a method of forming the exposed blood-contacting surface of a biomedical device, or a component thereof, comprising the steps of

(a) thoroughly dispersing no greater than 5 volume % of a polymer additive throughout at least 95 volume % of a base polymer to form a polymer mixture, the polymer additive comprising a first homopolymer chain component chemically bonded to at least a second homopolymer chain component

of a different type than the first component, the polymer additive being characterized by a  $\alpha_c$  less than that of the base polymer and the polymer mixture being characterized by a  $\alpha_c$  between 10 and 35 dyne/cm; and

(b) solidifying the polymer mixture and forming it into the blood-contacting surface of a biomedical device or component thereof.

In a second aspect there is provided a biomedical device or component thereof, including a blood-compatible, blood-contacting surface formed of a polymer mixture comprising at least 95 volume % of a base polymer and no greater than 5 volume % of a polymer additive comprising a first homopolymer chain component chemically bonded to at least a second homopolymer chain component of a different type than the first component, the polymer additive being dispersed throughout the base polymer and being characterized by a  $\alpha_c$  less than that of the base polymer, the polymer mixture being characterized by a  $\alpha_c$  between 10 and 35 dyne/cm.

The polymer mixtures of the invention may be used to provide a technique for lowering the surface free energy of a good structural polymer to convert a surface formed from such material from one which is blood incompatible to one which is blood compatible. As used herein, the term "base polymer" will refer to the polymer whose surface characteristics is so modified. Typical base polymers whose surfaces may be improved by the present technique include polyurethanes, polysulfones, polycarbonates, polyesters, polyethylene, polypropylene, polystyrene, poly(acrylonitrile-butadiene-styrene), polybutadiene, polyisoprene, styrene-butadiene-styrene block copolymers, styrene-isoprene-styrene block copolymers, poly-4-methylpentene, polyisobutylene, polymethyl-methacrylate, polyvinylacetate, polyacrylonitrile, polyvinyl chloride, polyethylene terephthalate, cellulose and its esters and derivatives, and the like.

The base polymer is of a type capable of being formed into a self-supporting structural body, a self-supporting film, or deposited as a coating onto a self-supporting body. The end use of the final product is the surface of a biomedical device or component thereof.

Another characteristic of the base polymer is that it includes a critical surface tension ( $\gamma_c$ ) in excess of that desirable for a blood contact surface and in excess of that of the polymer additive to be described below which reduces its  $\gamma_c$  value. As defined herein,  $\gamma_c$  measurements are performed by the direct method using a contact angle meter of the Kernco or Rame-Hart type and a series of seven solvents according to the Zisman procedure as set forth in A.W. Adamson, *Physical Chemistry for Surfaces* 339-357, 351 (3d Ed.). Measurements are made at room temperature using advancing angles on solvent cast films annealed at 60°C for four hours. The mean contact angles are fitted to a Zisman plot using a linear regression calculator program.

In accordance with the present invention, a base polymer of out below to lower its surface free energy. The polymer additive with a substantially lower  $\gamma_c$  value than that of the base polymer is

thoroughly dispersed into the base polymer while in fluid form to form a fluid polymer admixture.

Thereafter, the polymer admixture is solidified and formed into the blood-contacting surface of a biomedical device or component. The surface free energy of the polymer mixture is from 10 to 35 dyne/cm, while a preferred range is from 20 to 30 dyne/cm. An optimum range is 20-25 dyne/cm.

The polymer additive includes at least two different homopolymer chain components of different functional characteristics. One homopolymer chain, herein the "first component", has a relatively low  $\gamma_c$  value, less than that of both the base polymer and the second component and causes reduction in the  $\gamma_c$  of the polymer admixture as set out below. Such material typically has a tendency to exudate from the base polymer in admixture.

To prevent exudation, at least a second homopolymer chain, herein the "second component", is chemically bonded to the first component in the polymer additive to lower this tendency to exudate. The second component may be selected from the group of "hard block" polymer segments useful in the preparation of thermoplastic block copolymers as set out in A. Noshay and J.E. McGrath, *Block Copolymers Overview and Critical Survey* (Academic Press 1977). For biomedical applications, the hard blocks are characterized by a crystalline melting point greater than about 37°C and/or a glass transition temperature also greater than about 37°C. This second component has a higher surface free energy than the first one. For compatibility, the second component is preferably formed of a polymer of the same type as the base copolymer.

It has been found that the homopolymer component of the additive with the lowest  $\gamma_c$  value controls the  $\gamma_c$  value of the entire polymer additive. Thus, for example, if the first component has a  $\gamma_c$  value of 25 and the second component a  $\gamma_c$  value of 35, the total  $\gamma_c$  of the annealed additive is approximately 25.

Suitable homopolymers for the first component are those with a  $\gamma_c$  value in the desired range to lower the value of the base polymer to that desired for blood compatibility. Thus, it is preferable that such first component be characterized by a  $\gamma_c$  value less than 30 dyne/cm. One particularly effective homopolymer for this purpose is a polydimethylsiloxane with a  $\gamma_c$  on the order of 22 dyne/cm. Techniques for forming siloxane copolymers for use in the present invention are known, e.g., as described in W. Noll, *Chemistry and Technology of Silicones* (Academic Press, 1968). Suitable first component homopolymers include other polydialkylsiloxanes, polyfluoroalkyl alkylsiloxanes, polyalkylene oxides, polyolefins, polydienes and polyfluorocarbons.

Where the polymer admixture of the present invention is formed by mixing a preformed polymer additive of the foregoing type with base polymer, such polymer additive is suitably formed of block copolymers of alternating first and second components interlinked by chemical bonds in accordance with known techniques. For example, such block copolymers may be formed in accordance with the foregoing Noshay and McGrath publication. A suitable number of repeating units of each homopolym-

er of the first component is that sufficient to retain the  $\gamma_c$  value of the homopolymer as evidenced by retention of approximately the same glass transition temperature as its pure homopolymer. Typically, this number is on the order of 5 to 10 units or more. Similarly, there should be a sufficient number of repeating units of the second component in a segment so that the polymer additive is solid at room temperature.

The preparation of block copolymers (or multipolymers) may be performed by several procedures which differ in the degree to which the structure of the resulting product may be defined.

One procedure involves the coupling of two (or more) preformed blocks which are prepared in separate reactions prior to the coupling reaction. This procedure involves a very well defined structure if the coupling reaction precludes like blocks from reacting with themselves but only allows dissimilar blocks to couple to one another.

A slightly less well defined structure results if the two preformed blocks possess the ability (via the coupling reaction) to react with themselves as well as with the dissimilar block.

An even less well defined structure results when a single (or more) preformed block is coupled with a second block created during the coupling reaction. In this case the initial length of the preformed block is known (by virtue of the separate reaction used to prepare it) but the sequence distribution of the copolymer is not known exactly since both coupling and chain growth is possible in the reaction which produces the second block. Suitable methods of forming these and other such copolymers for use in the present invention are set out in the aforementioned Noshay and McGrath publication.

One unique specific mixture according to the present invention includes a block or graft copolymer of poly(dialkylsiloxane), specifically poly(dimethylsiloxane), as the first component and polyurethane as the second component. As used herein, the term "polyurethane" encompasses polyetherurethaneureas, polyether urethanes, polyester urethanes, or any of the other known polyurethanes, e.g., as set forth in Nyilas U.S. Patent 3,562,352 (Col. 2, line 66-Col. 3, line 37). This copolymer may be blended with any base polymer of desired physical properties. It is particularly effective for use with the same type of base polymer as the second component to provide improved compatibility.

If desired, three or more types of polymer chains may be employed in sequence so long as at least one type has a low  $\gamma_c$  value. An excellent terpolymer additive includes a block copolymer segment of the first and second components. The second component is linked to a segment formed of specifically either polyethylene oxide or polyethylene oxide-copolypropylene oxide, herein the "hydrophilic component". In this instance, the second component is a hard block with a crystalline melting point above 37°C or a glass transition temperature above 37°C. In a terpolymer of this type, the second component links the first component and the hydrophilic component. In one excellent terpolymer, the first compo-

5 nent is a poly(dialkylsiloxane), the second component is any of a broad group including polyurethane or polyurethane, and the hydrophilic component is either polyethylene oxide or polyethylene oxide-copolypropylene oxide. This terpolymer provides unexpectedly superior improvement in blood compatibility for a base polymer of the desired structural characteristics, such as a hard polymer of the same type as the second component.

10 Other forms of linked first and second homopolymers are of the graft copolymer type. Either the first or second copolymer may serve as the substrate upon which the pendant chains of the other type of homopolymer are grafted. The mode of forming graft copolymers is well known to those skilled in the polymer field. For example, see pp. 13-23 of the aforementioned Noshay and McGrath publication. The third mechanism in Table 2-1 illustrates a backbone structure suitable for grafting a hydroxyl-terminated polydimethylsiloxane (e.g., through a urethane linkage using a diisocyanate).

20 The ratio of first and second components in the polymer additive may vary to a considerable extent so long as there is sufficient amount of first component to reduce the  $\gamma_c$  value and sufficient amount of second homopolymer to prevent exudation of the polymer additive. It is preferable that the polymer additive include at least about 20 volume % of the first component. A suitable ratio is from 20 to 80 volume % of the first type of component and about 20 to 80 volume % of the second type of polymer component.

25 The total amount of polymer additive required to reduce the  $\gamma_c$  value of the base polymer to that desired for the polymer mixture is very low. For example, it has been found that less than 5 volume % and preferably less than 1 to 2 volume % of total polymer additive for silicone as the first component performs this function even though the first component typically comprises about half or less of the polymer additive. A suitable ratio of polymer additive to base polymers is on the order of 0.00002 to 2 volume % polymer additive based on the total polymer mixture. Experimental results have indicated that even though the polymer additive is initially mixed in bulk into the base polymer, it migrates to the surface to form an exceptionally thin (monomolecular) film which provides the desired surface characteristics. Sufficient polymer additive should be included to provide this uniform layer. The presence of an adequate amount of polymer additive is shown by a dramatic drop in the  $\gamma_c$  value of the polymer admixture to approximately that of the first component. While the required amount varies from system to system, it is generally less than 1 volume % of the first component based on the total polymer mixture. It is advantageous to use such low amounts of polymer additive as large amounts of the first component can be detrimental to the physical properties of the polymer mixture.

60 It has been found that the required minimum amount of polymer additive may be approximated by a knowledge of the film thickness of a polymer additive monolayer and the surface area to bulk volume ratio of the fabricated material. This is based

on the simplifying assumption that prior to surface saturation, essentially all of the polymer additive migrates to the surface. By simple calculation, this minimum amount may be precalculated based on this knowledge.

70 A number of techniques may be employed for mixing the polymer additive with the base polymer in accordance with the present invention. In one technique, both the base polymer and polymer additive are thermoplastic and are melted at elevated temperatures to perform the mixing. Thereafter, the polymer is solidified by cooling. If desired, the bulk polymer may be simultaneously processed into the desired final form. Alternatively, the material may be solidified for subsequent formation of the material into the desired form by thermoplastic methods such as injection molding and extrusion.

80 Another technique for mixing of the polymer additive and base polymer is by dissolving both of them in solvent and thereafter evaporating the solvent to form the solid product of the present invention. This product may also be subsequently processed by thermoplastic techniques if desired.

85 A third technique for forming the polymer admixture of the present invention is to polymerize in place with a vast excess (at least 95 volume %) of base polymer and a minor amount (no greater than 5 volume %) of a homopolymer additive of the first component type set out above. For example, low molecular weight polydimethylsiloxane having hydroxypropyl end groups is substituted for a small amount of polyetherglycol in the synthesis of a typical polyether urethane. Here the reaction product can contain enough silicone/polyurethane block copolymer to provide the desired surface characteristics. The concentration of the polymer additive would be so low that the great majority (at least 95 volume %) of the base polymer would not be linked to the additive polymer.

100 The polymer additive of the present invention must be thoroughly dispersed in the base polymer. For this purpose, it is preferable that the polymer additive be thermoplastic, soluble in organic solvents, and relatively uncrosslinked.

110 For most biomedical applications, the base polymers of the present invention should be thermoplastic so that they may be readily processed as desired. However, there are certain applications in which the polymers may be fabricated while fluid and thereafter solidified in the form of the fabricated part which cannot again be placed into the fluid form. For example, such base polymer may comprise thermosetting systems which are cured or vulcanized immediately following dispersion of the polymer additive. Such systems may include two component polyurethanes or epoxy resin systems.

120 One advantageous system in accordance with the present invention comprises an admixture of a polymer additive formed of a poly(dialkylsiloxane) segment chemically bonded to a polyurethane segment (e.g., in a block or graft copolymer) and mixed with a suitable base polymer, e.g., the same type of polyurethane as in the copolymer. A particularly effective system includes a polymer additive comprising a block copolymer of about 50 weight %



polydimethylsiloxane and 50 weight % polyurethane (specifically polyesterurethane) in a base polymer of polyurethane (specifically polyesterurethane). A suitable ratio is 99.9% polyester urethane base polymer and 0.1% of the block copolymer.

One mode of pretreating a base polymer to lower its surface free energy is believed to be effective with a base polymer which includes high energy end groups, specifically ones capable of hydrogen bonding or reacting with protein. In this instance, the base polymer is first fractionated to remove a lower molecular weight fraction and thereby may reduce the hydrogen bonding capacity of the remaining base polymer. Suitable techniques for accomplishing this are set out in Manfred J.R. Cantow, *Polymer Fractionation*, Academic Press (New York - London 1967). Such techniques include liquid chromatography, particularly gel permeation chromatography.

It has been found that variations in processing conditions which would otherwise affect the surface free energy to a significant extent may be minimized as a factor in systems of the present invention by the use of a short heat treatment following surface formation. For example, in a system comprising a base polymer of polyether urethane and a block copolymer of polyether urethane/polyalkylsiloxane, annealing for four hours at 75°C yields a  $\gamma_c$  value approximately equal to that of pure polysiloxane while it takes a considerably longer period of time to accomplish this objective at room temperature.

It has further been found that the polarity of the environment of formation affects the  $\gamma_c$  value of the surface. Thus an air equilibrated surface provides a lower  $\gamma_c$  than one which has been equilibrated in water.

The polymer mixtures of the present invention are particularly effective for use as a blood-contacting surface of a biomedical device or component. Such devices include auxiliary ventricles, intra-aortic balloons, and various types of blood pumps.

A further disclosure of the nature of the present invention is provided by the following specific examples of the practice of the invention. It should be understood that the data disclosed serve only as examples and are not intended to limit the scope of the invention.

#### Example 1

A typical synthesis of Polydimethylsiloxane-Polyurethane Block Copolymer.

To a 500 ml. four-necked flask equipped with stirrer, Dean and Stark trap, dropping funnel, drying tube, thermometer and inert gas inlet is placed a mixture of 50 ml. dimethylformamide and 140 ml. of tetrahydrofuran. The mixture is heated to reflux and approximately 40 ml. tetrahydrofuran is distilled off. The reaction mixture is cooled down and 12.513 gm (0.05 mole) of methylene bis (4-phenyl) isocyanate (MDI) is added to give a clear solution. From the dropping funnel 15.000 gm (0.015 mole) of 3-hydroxypropyl terminated polydimethylsiloxane (Mol. wt = 1,000) is added dropwise. The reaction mixture is heated at 105-100°C for 1 hour, followed by dropwise addition of 3.15 gm (0.035 mole) of 1-4,

butane diol over a period of 45 minutes. The polymerization is carried out for 15 minutes more, cooled down and precipitated by pouring into water in a blender. The slightly yellowish polymer is washed with water and finally with ethanol; dried in a vacuum oven at 50°C to afford = 30-31 gm of polymer (98-100%).  $[\eta]$  in tetrahydrofuran at 25°C is 0.19.

#### Example 2

By replacing some of the hydroxypropyl-terminated polydimethylsiloxane with polyethylene glycol, a polydimethylsiloxane/polyethylene oxide/polyurethane terpolymer is prepared.

80

#### Example 3

By replacing the DMF solvent with dimethylacetamide and substituting ethylene diamine for butane diol in Example 2 a polydimethylsiloxane/polyethylene oxide/polyurethane terpolymer is prepared.

85

#### Example 4

This example illustrates solution fabrication. A solution is prepared containing about 10 weight % mixture in a solvent system consisting of 90% tetrahydrofuran (vol/vol) and 10% dimethylformamide. The mixture consists of 99.9 weight % purified polyesterurethane and 0.1 weight % silicone/polyurethane block copolymer. The block copolymer consists of about 50 weight % polydimethylsiloxane and 50 weight % polyurethane from diphenylmethane diisocyanate and butane diol.

The solution is coated onto tapered stainless steel mandrels by multiple dipping. The solvent is allowed to evaporate and the film is removed from the mandrel. The resulting "balloon" is mounted on a pre-drilled catheter and is useful as a cardiac arrest device when placed in the descending aorta and inflated and deflated with CO<sub>2</sub> in counterpulsation to the heart.

The  $\gamma_c$  of the balloon film is 20 to 22 dyne/cm.

#### Example 5

Small test tubes are coated on their inner surface with two different polymer solutions (in THF) at 10 weight % concentration. One solution consists of polyetherurethane in the solvent. The second solution consists of 90 weight % solvent, 9.9 weight % polyetherurethane and 0.1 weight % copolymer additive. The copolymer consists of about 50% polydimethylsiloxane and 50% polyethylene oxide co-polypropylene oxide available from Petrarch Systems under the trade designation PS 072.

After solvent evaporation and about 16 hours equilibration in distilled water, fresh whole blood is placed in three tubes of each type.

Tubes coated with the unmodified polyetherurethane give mean whole blood clotting times of 39 minutes. Tubes coated with polyetherurethane containing the block copolymer additive give mean whole blood clotting times greater than 70 minutes.

The  $\gamma_c$  of the unmodified polyetherurethane is about 28 dyne/cm. The  $\gamma_c$  of the polyetherurethane containing the block copolymer additive is about 20





dyne/cm.

#### Example 6

This example illustrates thermoplastic fabrication.

- 5 A thermoplastic polyurethane is mixed in a single screw extruder at about 400°F with a block copolymer additive consisting of about 50 weight % polydimethylsiloxane and 50 weight % polyetherurethane such that the total silicone concentration of the mixture is 0.01 weight %. The mixture is extruded into the shape of tubing suitable for the transfer of blood. The tubing has a  $\gamma_c$  of about 21 dyne/cm after being annealed at 60°C for six hours.

#### Example 7

This example illustrates two component vulcanizing.

- 15 DuPont Adiprene L-167 polyetherurethane isocyanate terminated prepolymer is prepared according to the manufacturer's recommendations for a polyol cure, using a slight stoichiometric deficiency of butane diol/trimethylol propane mixture. While still liquid 0.1 weight % of the block copolymer additive of Example 1 is mixed with the reactants and an amine catalyst.

The resulting mixture is coated on a previously primed titanium connector and cured in an oven at 100°C.

- 20 The coated connector has a  $\gamma_c$  of about 20 dyne/cm. and is used in contact with blood to connect a conduit to a left ventricular assist device which is used to treat low cardiac output syndrome.

#### Example 8

- 35 A 4 mm tubular prosthesis was formed by coating a stainless steel mandrel with a polymer mixture consisting of 99.9 weight % poly(etherurethane urea) and 0.2 weight % polydimethylsiloxane/polyurethane block copolymer containing 50% polydimethylsiloxane, 50% polyurethane, in a dimethylacetamide solution. After solvent evaporation, the resulting tube was removed from the mandrel, extracted with distilled water at 60°C for 16 hours, dried and annealed for 4 hours at 60°C. After ethylene oxide sterilization the tube was sutured to the carotid artery of a goat.

- 40 Using an established radiolabeled platelet technique no enhancement in platelet turnover was measured relative to a sham experiment. A similar experiment easily detects changes in platelet turnover in polyvinylchloride tubing which is known to have low blood compatibility.

#### CLAIMS

- 55 1. A method of forming the exposed blood-contacting surface of a biomedical device, or a component thereof, comprising the steps of  
(a) thoroughly dispersing no greater than 5 volume % of a polymer additive throughout at least 95 volume % of a base polymer to form a polymer mixture, the polymer additive comprising a first homopolymer chain component chemically bonded to at least a second homopolymer chain component of a different type than the first component, the

polymer additive being characterized by a  $\gamma_c$  less than that of the base polymer and the polymer mixture being characterized by a  $\gamma_c$  between 10 and 35 dyne/cm; and

- 70 (b) solidifying the polymer mixture and forming it into the blood-contacting surface of a biomedical device or component thereof.

2. A method as claimed in claim 1 in which the first component *per se* is characterized by a  $\gamma_c$  less than 30 dyne/cm and a tendency to exude from mixtures with the base polymer and the second component lowers the tendency to exude.

3. A method as claimed in claim 1 in which the first component is a homopolymer selected from the group consisting of polydialkylsiloxanes, polyfluoroalkyl alkylsiloxanes, polyalkylene oxides, polyolefins, polydienes and polyfluorocarbons.

4. A method as claimed in claim 3 in which the first component is poly(dimethylsiloxane).

- 85 5. A method as claimed in claim 3 in which the first component is a poly(dialkylsiloxane), and the second component is a polyurethane.

6. A method as claimed in any one of the preceding claims in which the second component and the base polymer are formed of the same type of homopolymer.

7. A method as claimed in claim 1 in which the base polymer includes end groups capable of hydrogen bonding or reacting with protein, and which further comprises the step of fractionating the base polymer to remove a lower molecular weight fraction to reduce the hydrogen bonding capacity of the remaining base polymer prior to the dispersion step.

8. A method as claimed in any one of the preceding claims which further comprises the step of annealing the polymer mixture.

9. A method as claimed in any one of the preceding claims in which about 0.00002 to 2 volume % polymer additive is added to the base polymer based on the total polymer mixture.

10. A method as claimed in any one of the preceding claims in which the polymer additive comprises at least 20 volume % of the first component.

- 110 11. A method as claimed in claim 10 in which the polymer additive comprises 20 to 80 volume % of the first component and 20 to 80 volume % of the second component.

12. A method as claimed in any one of the preceding claims in which the polymer mixture is deposited as a film onto a biomedical device or component thereof.

13. A method as claimed in any one of the preceding claims in which the additive and base polymer are in molten form during dispersion and solidify on cooling.

14. A method as claimed in any one of claims 1 to 12 in which the polymer mixture is dissolved in solvent during mixing and the solvent is removed to solidify the polymer mixture.

15. A method as claimed in any one of the preceding claims in which the base polymer comprises a curable thermosetting fluid polymer which is solidified by curing.

- 130 16. A method as claimed in any one of the



preceding claims in which the polymer additive comprises a linear multiblock copolymer with blocks of at least the first and second components.

17. A method as claimed in any one of claims 1 to 15 in which the polymer additive comprises a graft copolymer with a substrate formed of the first component and pendant chains formed of the second component.

18. A method as claimed in any one of claims 1 to 15 in which the polymer additive comprises a graft copolymer with a substrate formed of the second component and pendant chains formed of the first component.

19. A biomedical device or component thereof, including a blood-compatible, blood-contacting surface formed of a polymer mixture comprising at least 95 volume % of a base polymer and no greater than 5 volume % of a polymer additive comprising a first homopolymer chain component chemically bonded to at least a second homopolymer chain component of a different type than the first component, the polymer additive being dispersed throughout the base polymer and being characterized by a  $\gamma_c$  less than that of the base polymer, the polymer mixture being characterized by a  $\gamma_c$  between 10 and 35 dyne/cm.

20. A biomedical device or a component thereof as claimed in claim 19 in which the first component *per se* is characterized by a  $\gamma_c$  less than 30 dyne/cm and a tendency to exude from mixtures with the base polymer and the second component lowers the tendency to exude.

21. A biomedical device or a component thereof as claimed in claim 19 in which the first component is a homopolymer selected from the group consisting of polydialkylsiloxanes, polyfluoroalkyl alkylsiloxanes, polyalkylene oxides, polyolefins, polydienes and polyfluorocarbons.

22. A biomedical device or a component thereof as claimed in claim 21 in which the first component is poly(dimethylsiloxane).

23. A biomedical device or a component thereof as claimed in claim 21 in which the first component is a poly(dialkylsiloxane) and the second component is a polyurethane.

24. A biomedical device or a component thereof as claimed in any one of claims 19 to 23 which is a blood compatible blood contact device or component thereof.

25. A biomedical device or a component thereof as claimed in any one of claims 19 to 23 wherein the blood compatible surface forms a blood contact layer adhered to the surface of a blood contact device.

26. A biomedical device as claimed in any one of claims 19 to 23 in which a portion of the polymer additive is in the form of a continuous layer on the surface of a blood contact device.

27. A biomedical device as claimed in any one of claims 19 to 23 in which a portion of the polymer additive comprises a linear multi-block copolymer with blocks of at least the first and second components on the surface of a blood contact device.

28. A biomedical device as claimed in any one of claims 19 to 23 in which a portion of the polymer

additive comprises a graft copolymer with a substrate formed of the first component and pendant chains formed of the second component on the surface of a blood contact device.

29. A biomedical device as claimed in any one of claims 19 to 23 in which a portion of the polymer additive comprises a graft copolymer with a substrate formed of the second component and pendant chains formed of the first component on the surface of a blood contact device.

30. A method of forming the exposed blood-contacting surface of a biomedical device, or components thereof substantially as hereinbefore described.

31. A biomedical device or component of a biomedical device substantially as hereinbefore described.

Amendments to the claims have been filed, and have the following effect:-

New or textually amended claims have been filed as follows:-

1. A method of forming the exposed blood-contacting surface of a biomedical device, or a component thereof, comprising the steps of  
(a) thoroughly dispersing no greater than 5 volume % of a polymer additive throughout at least 95 volume % of a base polymer to form a polymer mixture, the polymer additive comprising a first homopolymer chain component chemically bonded to at least a second homopolymer chain component of a different type than the first component, the first component having a  $\gamma_c$  less than that of both the base polymer and the second component, and the second component having a crystalline melting point greater than 37°C and/or a glass transition temperature greater than 37°C, the polymer additive being characterized by a  $\gamma_c$  less than that of the base polymer and the polymer mixture being characterized by a  $\gamma_c$  between 10 and 35 dyne/cm; and  
(b) solidifying the polymer mixture and forming it into the blood-contacting surface of a biomedical device or component thereof.

9. A method as claimed in any one of the preceding claims in which 0.0002 to 2 volume % polymer additive is added to the base polymer based on the total polymer mixture.

19. A biomedical device or component thereof, including a blood-compatible, blood-contacting surface formed of a polymer mixture comprising at least 95 volume % of a base polymer and no greater than 5 volume % of a polymer additive comprising a first homopolymer chain component chemically bonded to at least a second homopolymer chain component of a different type than the first component, the first component having a  $\gamma_c$  less than that of both the base polymer and the second component and the second component having a crystalline melting point greater than 37°C and/or a glass transition temperature greater than 37°C, the polymer additive being dispersed throughout the base polymer and being characterized by a  $\gamma_c$  less than that of the base polymer, the polymer mixture being characterized by a  $\gamma_c$  between 10 and 35 dyne/cm.



30. A method as claimed in claim 1 of forming the exposed blood-contacting surface of a biomedical device, or components thereof substantially as hereinbefore described.

- 5 31. A biomedical device or component of a biomedical device as claimed in claim 19 and substantially as hereinbefore described.

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